

A Randomized, Controlled Trial of Virtual Reality-Graded Exposure Therapy for Post-Traumatic Stress Disorder in Active Duty Service Members with Combat-Related Post-Traumatic Stress Disorder

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Abstract

Virtual reality (VR)-based therapy has emerged as a potentially useful means to treat post-traumatic stress disorder (PTSD), but randomized studies have been lacking for Service Members from Iraq or Afghanistan. This study documents a small, randomized, controlled trial of VR-graded exposure therapy (VR-GET) versus treatment as usual (TAU) for PTSD in Active Duty military personnel with combat-related PTSD. Success was gauged according to whether treatment resulted in a 30 percent or greater improvement in the PTSD symptom severity as assessed by the Clinician Administered PTSD Scale (CAPS) after 10 weeks of treatment. Seven of 10 participants improved by 30 percent or greater while in VR-GET, whereas only 1 of the 9 returning participants in TAU showed similar improvement. This is a clinically and statistically significant result ($\chi^2 = 6.74$, $p < 0.01$, relative risk 3.2). Participants in VR-GET improved an average of 35 points on the CAPS, whereas those in TAU averaged a 9-point improvement ($p < 0.05$). The results are limited by small size, lack of blinding, a single therapist, and comparison to a relatively uncontrolled usual care condition, but did show VR-GET to be a safe and effective treatment for combat-related PTSD.

Introduction

POST-TRAUMATIC STRESS DISORDER (PTSD) is a significant problem in warriors returning from combat in Iraq and Afghanistan. Reports have varied in regard to the exact percentage of Service Members affected,¹ but several studies have documented the severity of this problem,^{2,3} and events that may predict its outcome.⁴ A few single-group-design studies have reported on treatments that may help Service Members to recover from the disorder.⁵⁻⁷ However, despite the fact that the wars have now been ongoing since 2001, and that by 2008 over 1.6 million American troops had deployed to Iraq and Afghanistan,² there has been only one randomized, controlled, proof-of-concept study for Active Duty Service Members with PTSD, and that was conducted in survivors of the September 11

attacks on the Pentagon.⁸ Before this report, there were no randomized trials for PTSD in Active Duty Service Members who served in Iraq or Afghanistan. New treatment options are clearly needed for service members with PTSD.

PTSD related to any war has long suffered a dearth of successful clinical trials, possibly because of the difficulty in recruiting Service Members into research trials.⁹ Nevertheless, the evidence obtained from PTSD due to traumatic exposures other than combat has been used to benefit combat Veterans. Among the therapies for PTSD as a whole, the modes of treatment recognized as having the greatest amount of evidence in their favor are exposure therapies.^{10,11} Several randomized, controlled trials have demonstrated the benefit of exposure therapy in PTSD,^{12,13} and open label trials indicated that the same approach can be successfully used to treat combat PTSD.⁶

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Exposure therapies were developed in the 1920s as a means of treating phobias and other anxiety disorders. They are based on the idea that confronting, rather than avoiding, anxiety can help an individual to overcome anxiety. Exposure therapies include flooding, implosion therapy, systematic desensitization, prolonged exposure, and (according to some), Eye Movement Desensitization and Reprocessing.^{14,15} Exposure techniques differ in terms of how fear is confronted, for example, all at once (flooding) or in conjunction with relaxation techniques (systematic desensitization), and if exposure is done as a component of a purely behavioral therapy or part of mixed cognitive and behavioral treatment. The most commonly studied exposure therapy for PTSD is Prolonged Exposure, a technique that is usually classified as a cognitive behavioral therapy (CBT), and involves confronting anxiety by talking about the traumatic event(s) in session (imaginal exposure) and by confronting real-life reminders of the trauma outside of session (*in vivo* exposure).

One of the newer refinements to exposure therapy is the use of virtual reality (VR). VR-facilitated exposure therapy has been used to facilitate treatment of specific phobias^{16,17} and has recently emerged for the treatment of PTSD.^{18,19} VR exposure therapy allows a participant to confront a feared experience in a safe and controlled fashion.²⁰ Studies indicate that, for phobias, VR exposure therapy results in greater improvements in anxiety levels than treatments with imaginal exposure alone.¹⁷ Since that time, VR has been shown to be of benefit to victims of motor vehicle accidents,^{21,22} 9-11-2001 survivors,²³ and Veterans of the War on Terror.¹⁹ Different studies have applied VR in different ways, and not all studies have been successful, but a growing consensus suggests that VR-based therapies are helpful.²⁴ Despite this progress, randomized trials of VR-based therapies for PTSD have been sparse.

In 2005, the Office of Naval Research funded several studies of VR-based treatments for combat Veterans of Iraq/Afghanistan. As part of this, the authors participated in a treatment-development study²⁵ aimed at designing and developing VR software and testing hardware, software, and therapeutic methods that could potentially help Active Duty Service Members with combat-related PTSD or VR-graded exposure therapy (VR-GET).

VR-GET differs somewhat from that used previously for PTSD.¹⁸ For example, rather than adding VR to a traditional session of Prolonged Exposure,²⁶ VR-GET combines graded VR exposure with physiologic monitoring and skills training. This is designed to allow a participant to more fully confront and tolerate simulated memories and fears within the VR environment. In this way, VR-GET is similar to Stress Inoculation Training, another form of therapy that combines skills training with exposure to overcome PTSD.¹²

The theoretical advantage to the VR-GET approach is that it may allow a patient who is unable to identify or talk about a combat-related trauma to learn skills that can be applied to a number of anxiety-provoking situations. In particular, patients are trained to recognize and control excessive autonomic arousal and cognitive reactivity. This is intended to allow them to more fully confront difficult memories, intrusive thoughts, and feelings during therapy, and to be more fully engaged in their daily activities. As with other approaches to exposure therapy for PTSD,²⁶ VR-GET encourages engagement with, rather than avoidance of, trauma-

related triggers. Initial uncontrolled case studies suggested that VR-GET was a safe and effective treatment for combat-related PTSD.¹⁹

The next-stage study was to be a larger, multicenter, randomized, controlled trial of VR-GET. The logistics of performing this study within an Active Duty population turned out to be more difficult than expected, and only a smaller trial was completed. This article documents the outcome of that small, randomized trial, and also discusses the unique issues involved in attempting PTSD therapy trials in an Active Duty military environment. We hypothesized that patients with combat-related PTSD would be more likely to experience clinically significant improvements in VR-GET than treatment as usual (TAU).

Methods

Overview

This study was a randomized trial of VR-GET treatment versus a wait-list control condition in which participants received usual treatment for PTSD. All participants gave informed consent to participate, and all procedures were approved in advance by an Institutional Review Board. Procedures were also reviewed by an independent medical monitor. Due to an oversight, this clinical trial was not registered with clinicaltrials.gov until after the trial was completed. All treatment was conducted at U.S. Navy medical facilities, and adhered to all federal and military guidelines regarding the treatment of Service Members and of research participants. Treatment success was based on the ability to show a clinically meaningful improvement (30 percent or greater reduction in PTSD symptoms on the Clinician Administered PTSD Scale [CAPS]²⁷) over the course of 10 weeks.

Study sites

The study was conducted at Naval Medical Center San Diego (NMCS D) and Naval Hospital Camp Pendleton (NHCP). NMCS D serves as the primary, mental-health treatment facility for four Navy and two Marine bases in San Diego, as well as the tertiary care and psychiatric hospitalization site for Service Members in the Western United States and Pacific Rim. Members of all branches of the US Armed Forces, as well as their family members, receive care at NMCS D. NHCP is located on the Marine Corps Base Camp Pendleton, which is the largest Marine Corps base in the world. As is the case at NMCS D, members of any branch of the Armed Forces are eligible for treatment at NHCP, but as a practical matter, most of the patient population consists of Marines and Sailors.

Study participants

Participants for the study were all Active Duty Service Members who had been diagnosed by a military mental health professional as having PTSD related to service in Iraq or Afghanistan. Participants had to be willing and able to give informed consent to participate. Participants were excluded if they were actively suicidal, homicidal, or psychotic, or if they had a diagnosis of alcohol dependence that did not show signs of at least early remission. Participants could elect to leave the study and receive traditional treatment for their PTSD at any time. Participants were recruited by flyers posted at military bases and by contact with military mental

health providers. Owing to their Active Duty Status, participants could not be paid or compensated for their contribution to the study. In advance of taking part in evaluation for the program, participants were made aware that under military regulations, privacy could not be guaranteed in regard to the result of the evaluation or treatment.

Participant assessment and randomization

Participants were screened by independent assessors to determine eligibility and provided informed consent for participation. They met with a licensed provider at the end of the assessment to determine safety for study entry and confirm a diagnosis of PTSD. Participants who met initial screening criteria were further evaluated by the CAPS,²⁷ review of existing medical records, structured psychiatric interview (Mini International Neuropsychiatric Interview),²⁸ and other assessment instruments. Participants had to meet criteria for PTSD within the past month on the Mini-International Neuropsychiatric Interview (with symptoms rated over the last month) and have a CAPS score of at least 40 (with symptoms rated over the past week). Patients were to be excluded if they had another condition that the therapist considered might make it unsafe for the participant to enter VR-GET or traditional treatment for PTSD, but, as a practical matter, this exclusion criteria never came into play. At the end of the baseline assessment, qualified participants drew a slip of paper out an envelope, which gave them an equal chance of receiving either treatment condition. Ten participants were assigned to VR-GET and an equal number to TAU. Neither the participant nor the assessor was blinded to treatment condition in the followup interview, but the assessor was independent of the therapists who provided treatment. An appointment was set at the completion of the initial assessment for the participant to be re-assessed 10 weeks later, regardless of participation in treatment. Participants also gave permission to review their military medical records to determine the mental health treatment they received. Participants who missed the post-assessment were rescheduled for assessment. Although the goal was always to get the participants in for reassessment as close to 10 weeks after baseline as possible, re-assessment for some did go out as far as 36 weeks past the intended date.

VR-GET treatment and VR equipment

Both the therapy methods and the VR equipment have been described in detail earlier.^{25,29} In brief, therapy was conducted according to a treatment manual written for the study,²⁵ and which is available on the Web (www.navypsych.com). Therapy was conducted by a licensed psychologist who had previously treated participants during the treatment-development phase of the project.^{19,29} Participants met with the therapist up to twice a week (this was the planned therapeutic frequency, although due to work-related issues, the session frequency was more typically once a week) for up to 10 weeks. In the first session of treatment, the therapist met with the participant, explained the rationale for therapy, conducted an intake interview and trauma history, and taught the participant aspects of meditation and attentional control (noticing distractions, letting them go, and refocusing on the task at hand), in combination with autonomic control using the J&J Engineering Biofeedback system. A relaxation CD was given to participants to practice with between

sessions (Jon Cabot Zinn & Andrew Weil, Meditation for Optimum Health, Sounds True, Boulder, CO). Attentional and autonomic control training were reviewed in the second session, and the participant was asked to practice these skills during recall of his or her trauma. Additionally, during the first two sessions, the participants were asked to discuss their PTSD symptoms and they were asked to, "tell their stories about their sentinel (i.e., most traumatic) events during their combat tour or tours." PTSD was discussed as a normal response to an abnormal situation.

In the third session and beyond, the participant was exposed to a VR simulation of Iraq or Afghanistan that approximated the participant's most salient traumatic experience. Three-dimensional visual scenarios with relevant sounds of wartime situations were viewed through a head mounted display. Movement of the head mounted display and a joystick controller allowed the participant to move about and interact with the simulated world. The graphics' quality was not photo-realistic, but similar to what might be experienced in a high-quality, modern video game. The therapist could vary the intensity of combat-related sights and sounds within the simulation, and direct the patient to relevant scenarios, including a base camp, battlefield, Iraqi marketplace, house-to-house search, or a military convoy coming under attack. Depending upon the patient reactivity (as determined by physiological monitoring and Subjective Units of Distress), the stressfulness of the experience was increased gradually by increasing the realism and violence in the VR simulation while the participant narrated parts of his or her traumatic experience. In each session, the participant was monitored for the ability to face fear and anxiety, and their ability to regain attentional control to more fully tolerate the scenario. No specific cutoff was used for either Subjective Units of Distress or physiologic reactivity. Cognitive restructuring was conducted at the end of each session, and participants were consistently monitored for suicidal thinking or other dangerous outcomes.

Participants who were assigned to the VR-GET condition were asked not to engage in any other form of individual psychotherapy, although they could continue in psychotherapy groups and in psychiatric medication management.

TAU condition

Participants assigned to TAU could receive any of the regular services available at NMCS and NHCP. These facilities offer a full spectrum of PTSD treatment, including prolonged exposure, cognitive processing therapy, Eye Movement Desensitization and Reprocessing, group therapy, psychiatric medication management, substance rehab, inpatient services, or a combination of these. As a practical matter, TAU patients who engaged in therapy likely received combination approaches that, as part of routine clinical practice, did not adhere strictly to a particular treatment protocol. For this reason it was not possible to identify the specific mode of therapy that a patient received. Rather, only the total number of mental health visits was tracked. This was determined by review of the participants' electronic, military medical record.

Primary outcome measure

The goal of the study was to identify which treatment resulted in a greater percentage of individuals with a clinically meaningful reduction in PTSD. This was determined by

examining differences in CAPS scores at initial assessment and then at the post-treatment assessment in VR-GET versus TAU. The CAPS is a rating scale for PTSD that corresponds with the 17 symptoms of PTSD listed in DSM-IV. Each of these symptoms is rated for frequency and severity by an independent rater who performs a trauma interview with the participant. The CAPS can be rated over a variety of time periods, and, in this study, a 1-week period of symptoms was rated. The CAPS takes about 45 min to administer. All CAPS raters in this study had received prior training in this method and had regular checks for inter-rater reliability. In 30 co-rated assessments the inter-rater Pearson correlation was 0.97. Scores on the CAPS can range from 0 to 136, with scores above 40 considered clinically significant for PTSD.³⁰ An improvement of 30 percent or greater on the CAPS is considered a clinically significant change.³⁰

Statistical analysis

Participants were classified according to if they did or did not have a 30 percent or greater reduction in their PTSD symptoms based on the CAPS.³⁰ Proportion of responders in VR-GET versus TAU was compared by chi-square, with Yates correction. Relative risk and 95 % confidence interval were calculated using the approximation of Katz.

For demographic information, categorical variables were compared by Fisher exact test, and continuous variables were compared by Student's *t*-test. Student's *t*-tests were used to compare the number of weeks to followup, and the total number of mental health encounters. As a back up to the primary, chi-square analysis, repeated measures analysis of variance was used to examine Group×Time changes in CAPS scores.

Results

Participant participation

Twenty participants met inclusion criteria for the study. Of these, 10 were randomly assigned to VR-GET and 10 to TAU. Demographics were generally similar at baseline (Table 1). All participants participated in treatment, with TAU participants averaging just under 14 visits in 10 weeks, and VR-GET participants receiving, on average, just over 11 total mental health visits, about 8 of which were actually for VR-GET treatments (Table 1). Post-treatment assessment often did occur at exactly the 10-week mark as was initially intended; however, all but one participant (who was in the TAU group) did eventually return to complete a post-treatment assessment (Table 1). The one participant who failed to return for post-treatment assessment did not fall outside of the 95 % interval on any measured score at baseline. We were not able to definitively determine why this participant did not return, but it is believed that he had left the military and moved. To our knowledge, no participants left the study due to adverse events, and no participant had worsening of symptoms to the point that hospitalization or other emergency intervention was needed. None of the VR-GET participants were unable to tolerate the VR environment.

Response to treatment

All 10 participants who participated in VR-GET were assessed with the CAPS at the postassessment. Seven (70 percent)

TABLE 1. DEMOGRAPHIC VARIABLES AT BASELINE AND AMOUNT OF TREATMENT OVER 10 WEEKS

	VR		TAU	
	Mean	Range	Mean	Range
N	10	NA	10	NA
Age	28	22–43	28.8	21–45
Male gender	90%	NA	100%	NA
Navy	60%	NA	30%	NA
Enlisted	100%	NA	90%	NA
Failed previous treatment	80%	NA	90%	NA
On Meds	90%	NA	90%	NA
Prior Deployments	3.3	1–8	1.4	1–3
#Mental Health Sessions (not including VR)	3.5	1–7	13.8	3–38
# Sessions VR	8.8	4–20	NA	
#Weeks to postassessment	13.6	10–22	16.9	10–46

"Failed previous treatment" indicates that the individual continued to meet entry criteria for the study (PTSD by MINI and CAPS >40) despite at least 10 weeks of previous therapy or psychiatric medication intervention. The number of mental health sessions was determined by record review from the participants' electronic, military medical record. Any visits to mental health or deployment health psychology clinics were counted regardless of the type of visit. Primary care and other general medical visits were not included. Visits to mental health providers that may have occurred outside the military medical system were not included.

VR, virtual reality; PTSD, post-traumatic stress disorder; TAU, treatment as usual; CAPS, Clinician Administered PTSD Scale; MINI, Mini-International Neuropsychiatric Interview; NA, not applicable.

of these showed a 30 percent or greater improvement in the CAPS. Of the 10 participants who received TAU, 1 did not return to complete a CAPS at postassessment. One (11.1 percent) of the 9 returning participants receiving TAU showed >30 percent improvement on the CAPS. Chi-square for the treatment response comparison between VR-GET and TAU was 6.74, $p < 0.01$. With Yates correction $\chi^2 = 4.54$, $p < 0.05$, relative risk was 3.21, with 95 % confidence interval 1.18 to 8.72.

Participants in both VR-GET and TAU showed a wide variation in their overall response to treatment (Table 2). Two-way analysis of variance showed a significant effect of time (pre- vs. post-treatment, $p < 0.001$), but not group ($p > 0.05$). There was a significant time-by-group interaction ($p < 0.05$).

There was no significant difference between VR-GET and TAU mean CAPS score before or after treatment (Table 2), but there was a significant difference in the mean CAPS change score over the course of treatment (35.4 vs. 9.4, $p < 0.05$).

Discussion

This study documents a randomized, controlled trial of a VR-GET for combat PTSD, and the first randomized trial of any sort for combat PTSD in Active Duty Service Members who served in combat operations in Operation Iraqi Freedom (Iraq) or Operation Enduring Freedom (Afghanistan). Results indicate that 70 percent of participants who received VR-GET showed a clinically significant (>30 percent) improvement in their PTSD symptoms after 10 weeks of treatment. This was a significantly ($p < 0.05$) greater percentage than the 12.5 percent of participants who showed clinically significant responses in usual treatment.

TABLE 2. TRAUMA, SYMPTOMS, AND TREATMENT RESPONSE FOR EACH PARTICIPANT

	<i>Index trauma</i>	<i>Duration of symptoms</i>	<i>Pretreatment CAPS</i>	<i>Post-treatment CAPS</i>	<i>Point change</i>	<i>% improved</i>	<i>Weeks between assessments</i>
VR-GET							
	Shot	8 months	68	7	61	90%	11
+	Ambush	3 years	83	11	72	87%	10
	Ambush	3 years	70	11	59	84%	20
	IED blast	4 years	49	9	40	82%	24
	Mortar attack	3 years	96	54	42	44%	16
	Suicide bomber	1 year	87	54	33	38%	11
	IED blast	1 year	87	57	30	34%	12
	Firefight	6 months	100	87	13	13%	15
	Mortar attack	1 year	113	103	10	9%	11
	Military medical trauma	2 years	82	88	-6	-7%	11
Mean			83.5	48.1	35.4	47.3%	14.1
SD			18.1	36.9	24.7	36.2%	4.7
SEM			5.7	11.7	7.8	11.5%	1.5
TAU							
	IED blast	2 years	76	0	76	100%	46
	Close combat	3 years	73	60	13	18%	15
	IED blast	5 months	78	67	11	14%	21
	IED blast	1 year	72	63	9	13%	11
	Fire fight	1 year	74	67	7	9%	11
	Suicide bomber	3 years	115	119	-4	-3%	18
	Fire fight	2 years	72	78	-6	-8%	11
	Civilian casualties	3 years	91	101	-10	-11%	10
	Civilian casualties	2 years	85	96	-11	-13%	10
	Bridge collapse	9 months	92	N/A	N/A	N/A	Dropout
Mean			82.8	72.3	9.4	13.1%	17.0
SD			13.6	33.8	26.6	34.6%	11.6
SEM			4.5	11.3	8.9	11.5%	3.9

Positive numbers for change indicate improvement. Subjects are ordered according to % improvement. + indicates the one, female participant in the study.
 GET, graded exposure therapy.

The response rates seen here are similar to those reported in previous, single-group design studies that have investigated VR-based therapies,^{7,29} as well as for other forms of exposure therapy for PTSD.¹³ An Institute of Medicine review concluded that generally speaking therapies based on exposure models have the greatest degree of evidence supporting their use in treating PTSD.¹⁰ However, direct comparisons of treatment effectiveness between noncombat and combat PTSD are difficult to make. The Institute of Medicine also concluded that insufficient evidence existed to determine if combat PTSD did or did not respond in the same way as when the disorder was caused by other means.¹⁰ Other studies suggest that combat PTSD is indeed more complex and difficult to treat.³¹ Some treatments, such as selective serotonin reuptake inhibitors, which demonstrated efficacy in noncombat, have often failed to demonstrate clear efficacy in combat Veterans.³² As shown in Table 1, most participants in this study were being prescribed psychotropic medications and had failed at least one previous treatment trial. Therefore, these results were obtained in a sample with documented treatment resistance.

The specific treatment applied here used VR simulation to allow Service Members to challenge their wartime fears and anxiety in a safe and interactive environment. The theoretical advantages to this method are that it allows a greater degree of control over the manner in which anxiety-producing

situations are confronted compared to imaginal or *in vivo* exposure. Physiologic monitoring and arousal control training were used to enhance the tolerability and monitoring for safe levels of arousal.

Whereas definitively determining what specific components of therapy are essential to outcome is beyond the scope of this study, it is important to note that a feared potential consequence of VR treatment did not happen. No one in this study became significantly worse after VR-GET treatment. Further, no one had to stop a VR session due to discomfort caused by the equipment (cybersickness). In general, this is in line with other previous studies of VR, which have found that under the proper supervision of a trained therapist, the simulated trauma is tolerable to even severely traumatized patients.³³ Overall, this study adds to the literature supporting the idea that VR is an effective treatment for anxiety disorders.¹⁶ It also suggests that VR-GET may be an effective treatment for combat-related PTSD.

Although these initial results are promising, the study conducted here was limited in a number of ways. It was small, not blinded, had a single therapist, did not include protocol-adherence measures, used a control group that allowed for a wide variety of possible treatments, and did not include long-term followup. The followup period did turn out to be much longer than initially intended, as many participants did not return at the 10-week mark. Some

participants in the TAU condition went out as far as 46 weeks before returning for their re-assessment. It is unclear how the difference in followup period affected the overall results. Presumably, a longer followup interval would have allowed for more treatment and greater recovery, but is also possible that participants tended to return at the point at which they wanted to ask for additional help. Overall, the difference in followup times between the groups was not statistically significant. However, for an individual participant, a nonstandard followup time may have influenced results.

This study was originally conceived as a much larger treatment trial, but difficulties with recruiting and performing therapy required the formation of more modest goals. Active Duty populations present a particular challenge to research. This is reflected in the fact that, despite extensive funding efforts aimed at the issue, few studies for treatment in this population have been published. Those studies that have been published are often plagued by low sample sizes,⁸ high dropout rates,⁷ and the issue of mental health stigma in the military.⁴ In general and especially at a time of war, Active Duty Service Members are in a constant state of flux (changing duty stations, changing duties at their current duty station, changing leadership, etc.), which adds to the challenge of recruitment and retention in research studies. Also, the Active Duty participants cannot be reimbursed for the time they participate in the research study.

Another barrier to recruiting Active Duty Service Members to participate in an intervention study includes their access to free medical care, making it unlikely they will volunteer if they may be randomized to a treatment that is perceived as being less than optimal treatment. In fact, an earlier design of this study had control group participants assigned to a CBT group; however, that design failed because so few participants were willing to participate. Of the few who did, none who were assigned to the CBT group control attended the CBT sessions. Taking time to establish relationships with providers, commanders, and potential participants eventually allowed a treatment population to be recruited. We also changed the TAU group to a wait list control so that participants who came in specifically seeking VR-GET knew they would eventually be offered the treatment of their choice (i.e., VR-GET).

Scientifically, TAU is a less-than-ideal control group because of the extreme variability in what may be included in usual treatment. Practically, however, the TAU control was acceptable to Service Members and their commanders. The study was conducted at facilities where providers are trained in all modalities of treatment recommended by Department of Defense and Veterans Affairs guidelines.¹¹ This would include Prolonged Exposure Therapy, Eye Movement Desensitization and Reprocessing, Cognitive Processing Therapy, and pharmacology for PTSD. Presumably, however, by the time Service Members arrive at a research study, they have likely already failed some form of traditional treatment and may not wish to participate in what is already available. Interestingly, all participants in the TAU group here did come to some form of mental health treatment (Table 1), although the number of visits did vary widely, as did the response to treatment.

Since we did not control what was done in the TAU group, this study should not be taken to mean that VR-GET is superior to any other specific form of treatment. We are aware of only one randomized comparison of VR versus another spe-

cific treatment for PTSD, a trial of 11 Vietnam Veterans that compared VR Exposure to Presence Centered Therapy. This trial was not able to detect statistically significant differences, likely due to low power.³⁴ Likewise, a nonrandomized clinical comparison in Service Members who received exposure therapy with or without VR failed to show statistically significant differences between the treatments.³⁵ However, that study was both underpowered and presented an unusual situation since the treatment was actually done in Iraq. TAU is a higher level of care than a wait-list control without treatment, which has been used as comparison group in many trials of PTSD, but further work will be needed to see if VR therapies are really superior to other, specific interventions.

Followup in this study was limited. Other single-group studies of VR-based therapies for PTSD have indicated that symptom improvements persist or continue for at least 3 months.⁷ Longer-term followups are clearly needed. Also needed is information on the practical implications of improvements in PTSD symptoms. Many times, an improvement in symptoms may mean that a Service Member is eligible to deploy again to a combat zone. Even for those who are exiting the service, an improvement may mean a lower disability rating and thus a potential reduction in future income. Careful monitoring is needed to make sure that treatments that improve symptoms of PTSD also improve the overall health and lives of Service Members.

Conclusions

The findings here indicated that Service Members with PTSD related to service in Iraq or Afghanistan were more likely to improve if they received VR-GET than if they received TAU. Like most aspects of mental health, a one-size-fits-all approach is unlikely to emerge. Future work should determine which approaches work best for which patients. In the meantime, VR-GET may present one avenue by which some Service Members with PTSD may be offered relief.

Disclosure Statement

Drs. Mark and Brenda Wiederhold are part owners of, and Drs. Wood, Webb-Murphy, and Spira have previously been employed by, Virtual Reality Medical Center which develops and sells the Virtual Reality system described in this work.

References

1. Sundin J, Fear NT, Iversen A, et al. PTSD after deployment to Iraq: Conflicting rates, conflicting claims. *Psychological Medicine* 2009; 12:1–16.
2. Tanielian T, Jaycox LH, ed. (2008) *Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery*. Santa Monica, CA: Rand Corporation Monographs.
3. McLay RN, Deal WE, Murphy JA, et al. On-the-record screenings versus anonymous surveys in reporting PTSD. *American Journal of Psychiatry* 2008; 165:775–776.
4. Hoge CW, Castro CA, Messer SC, et al. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *New England Journal of Medicine* 2004; 351:13–22.
5. Rauch SA, Defever E, Favorite T, et al. Prolonged exposure for PTSD in a Veterans Health Administration PTSD clinic. *Journal of Traumatic Stress* 2009; 22:60–64.

6. Ready DJ, Thomas KR, Worley V, et al. A field test of group based exposure therapy with 102 veterans with war-related posttraumatic stress disorder. *Journal of Traumatic Stress* 2008; 21:150–157.
7. Rizzo AA, Difede J, Rothbaum BO, et al. VR PTSD exposure therapy results with active duty OIF/OEF combatants. *Studies in Health Technology and Informatics* 2009; 142:277–282.
8. Litz BT, Engel CC, Bryant RA, et al. A randomized, controlled proof-of-concept trial of an Internet-based, therapist-assisted self-management treatment for posttraumatic stress disorder. *American Journal of Psychiatry* 2007; 164: 1676–1678.
9. Bender B. (2009) *Veterans forsake studies of stress, stigma impedes search for remedies*. Boston Globe, August 24, p. 1, Boston, MA.
10. Berg AO, Breslau N, Goodman SN, et al.; and the Institute of Medicine Study Staff. (2008) *Treatment of posttraumatic stress disorder, an assessment of the evidence. Committee on treatment of posttraumatic stress disorder, Board on Population Health and Public Health Practice, Institute of Medicine of The National Academies*. Washington, DC: The National Academies Press.
11. Carlson EB, Curran E, Friedman MJ, et al. (2004) *Iraq war clinician guide*. 2nd ed. Boston MA: Department of Veterans Affairs National Center for PTSD.
12. Foa EB, Rothbaum BO, Riggs DS, et al. Treatment of post-traumatic stress disorder in rape victims: A comparison between cognitive-behavioral procedures and counseling. *Journal of Consulting and Clinical Psychology* 1991; 59: 715–723.
13. Bradley R, Greene J, Russ E, et al. A multidimensional meta-analysis of psychotherapy for PTSD. *American Journal of Psychiatry* 2005; 162:214–227.
14. Keane TM. The role of exposure therapy in the psychological treatment of PTSD. *National Center for PTSD Clinical Quarterly* 1995; 5:1–6.
15. Rogers S, Silver SM. Is EMDR an exposure therapy? A review of trauma protocols. *Journal of Clinical Psychology* 2002; 58:43–59.
16. Rothbaum BO, Hodges LF. The use of virtual reality exposure in the treatment of anxiety disorders. *Behavior Modification* 1999; 23:507–525.
17. Wiederhold BK, Jang DP, Gevirtz RG, et al. The treatment of fear of flying: a controlled study of imaginal and virtual reality graded exposure therapy. *IEEE Transactions on Information Technology in Biomedicine* 2002; 6:218–223.
18. Rothbaum BO, Hodges LF, Ready D, et al. Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. *Journal of Clinical Psychiatry* 2001; 62:617–622.
19. Wood DP, Murphy JA, Center KB, et al. Combat related post traumatic stress disorder: a multiple case report using virtual reality graded exposure therapy with physiological monitoring. *Studies in Health Technology and Informatics* 2008; 132:556–661.
20. Wiederhold BK, Wiederhold MD. (2004) *Virtual reality therapy for anxiety disorders: Advances in education and treatment*. New York: American Psychological Association Press.
21. Beck JG, Palyo SA, Winer EH, et al. Virtual reality exposure therapy for PTSD symptoms after a road accident: An uncontrolled case series. *Behavior Therapy* 2007; 38:39–48.
22. Walshe DG, Lewis EJ, Kim SI, et al. Exploring the use of computer games and virtual reality in exposure therapy for fear of driving following a motor vehicle accident. *Cyberpsychology and Behavior* 2003; 6:329–334.
23. Difede J, Cukor J, Jayasinghe N, et al. Virtual reality exposure therapy for the treatment of posttraumatic stress disorder following September 11, 2001. *Journal of Clinical Psychiatry* 2007; 68:1639–1647.
24. Wiederhold BK, Wiederhold MD. Virtual reality for post-traumatic stress disorder and stress inoculation training. *Journal of Cybertherapy Rehabilitation* 2008; 1:23–35.
25. Spira JL, Pyne JM, Wiederhold BK. (2006) *Experiential methods in the treatment of combat PTSD*. In Figley CR, Nash WP, eds. *For those who bore the battle: Combat stress injury theory, research, and management*. New York: Routledge (EDP: October, 2006).
26. Foa E, Hembree E, Rothbaum BO. (2007) *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences therapist guide*. Oxford: University Press.
27. Blake DD, Weathers FW, Nagy LM, et al. The development of a Clinician-Administered PTSD Scale. *Journal of Traumatic Stress* 1995; 8:75–79.
28. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry* 1998; 59 Suppl 20:22–33.
29. Wood DP, Murphy J, Center K, et al. Combat-related post-traumatic stress disorder: A case report using virtual reality exposure therapy with physiological monitoring. *Cyberpsychology and Behavior* 2007; 10:309–315.
30. Weathers FW, Keane TM, Davidson JR. Clinician-administered PTSD scale: A review of the first ten years of research. *Depression and Anxiety* 2001; 13:132–156.
31. Prigerson H, Maciejewski P, Rosenheck R. Combat trauma: Trauma with highest risk of delayed onset and unresolved posttraumatic stress disorder symptoms, unemployment, and abuse among men. *Journal of Nervous and Mental Disease* 2001; 189:99–108.
32. Friedman MJ, Marmar CR, Baker DG, et al. Randomized, double-blind comparison of sertraline and placebo for post-traumatic stress disorder in a Department of Veterans Affairs setting. *Journal of Clinical Psychiatry* 2007; 68:711–720.
33. Murphy J, Center K, Wood D, et al. Relationship of cyber-sickness to post traumatic stress disorder and mild traumatic brain injury in military personnel enrolled in a virtual reality graded exposure therapy treatment trial. Poster presentation at Cybertherapy-13, June 2008, Lago Maggiore, Italy.
34. Ready DJ, Gerardi RJ, Bakscheider AG, et al. Comparing virtual reality exposure therapy to present-centered therapy with 11 U.S. Vietnam veterans with PTSD. *Cyberpsychology and Behavior Social Network* 2010; 13:49–54.
35. McLay RN, McBrien C, Wiederhold MD, et al. Exposure therapy with and without virtual reality to treat PTSD while in the combat theater: A parallel case series. *Cyberpsychology and Behavior Social Network* 2010; 13:37–42.

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